

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

REC'D 24 SEP 2004

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Applicant's or agent's file reference PZ02106 PCT		FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/GB 03/05576		International filing date (day/month/year) 19.12.2003	Priority date (day/month/year) 20.12.2002
International Patent Classification (IPC) or both national classification and IPC C07B59/00			
Applicant AMERSHAM PLC			
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>			
<p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the opinion</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p>			
Date of submission of the demand 18.06.2004		Date of completion of this report 27.09.2004	
Name and mailing address of the international preliminary examining authority:  European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016		Authorized Officer Diederen, J Telephone No. +31 70 340-1097 	

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB 03/05576

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-19 as originally filed

Claims, Numbers

1-14 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:
- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.
4. The amendments have resulted in the cancellation of:
- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:
5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/GB 03/05576**

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 1-3 (in part), 7 (in part), 8(in part), 12-14 (in part)
because:
 - ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):
 - ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
 - ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the said claims Nos. 1-3, 7,8,12-14

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the Standard.
- ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-14
	No: Claims	
Inventive step (IS)	Yes: Claims	1-14
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-14
	No: Claims	

2. Citations and explanations

see separate sheet

Reference is made to the following document:

D1: LAURENT MARTARELLO ET AL.: "Synthesis of syn- and anti-1-Amino-3-[18F]fluoromethyl-cyclobutane-1-carboxylic Acid (FMACBC), Potential PET Ligands for Tumor Detection" J. MED. CHEM., vol. 45, 26 April 2002 (2002-04-26), pages 2250-9, XP002276531

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

For claims 1-3, 7, 8, 12-14 (all in part) no international search report was issued. Consequently, no examination will be carried out on these claims, except for the subject-matter which was searched : i.e. the subject-matter related to compounds of Formula (Ia), methods, kits, cartridges and processes in which a compound of Formula (Ia) is used.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Novelty (Article 33(2) PCT)

The subject-matter of the present application meets the requirements of Article 33(2) PCT with respect to novelty.

The closest prior art is disclosed in D1, wherein FMACBC is synthesized. The subject-matter of claim 1 is novel over D1, as the process of claim 1 includes solid phase synthesis, which was not disclosed in the prior art. Therefore is claim 1 novel.

The compounds of Formula (Ia) are novel as the cyclobutane amino acid was never linked to a solid support. Therefore is claim 8 (with respect to compounds of Formula (Ia)) and 9 novel.

As the compounds of Formula (Ia) are novel, the kits cartridges and methods of claims 12-14 comprising these compounds are also novel.

Inventive Step (Article 33(3) PCT)

The subject-matter of the present application meets the requirements of Article 33(3) PCT with respect to inventive step.

The closest prior art is disclosed in D1, wherein FMACBC is synthesized. The main difference of this disclosure and the subject-matter of claim 1 of the present application is that the compound is produced with the help of solid phase synthesis in the present application and that in the prior art, the compound is produced without.

The advantages of solid phase synthesis are known to a person skilled in the art. The problem to be solved by the applicant was to provide an alternative solution for the synthesis of compounds of Formula (Ia). A skilled person would not, starting from D1, come to the solution of the present application as there is no indication in the prior art to use solid phase synthesis. Therefore is the subject-matter of claims 1-7 (with respect to compounds of Formula (Ia)) regarded to involve an inventive step according to Article 33(3) PCT.

The compounds claimed in claim 8-11 are used in an inventive process to prepare ¹⁸F-labelled tracer compounds. The subject-matter of these claims (with respect to compounds of Formula (Ia)) are therefore regarded to involve an inventive step according to Article 33(3) PCT.

Claims 12-13 deal with kits and cartridges comprising the inventive compounds of Formula (Ia). Therefore is the subject-matter of claims 12 and 13 (with respect to compounds of Formula (Ia)) considered to involve an inventive step according to Article 33(3) PCT.

Claim 14 deals with a method for obtaining a diagnostic PET image comprising using a kit or cartridge according to claim 12 or 13. This claim is considered inventive as the active ingredient (compounds of Formula (Ia)) is used.